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Reply

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We want to thank Dr. Pang et al. for their interest and important remarks regarding our article. In our recently published investigation we reported intra-platelet (IP) 5-hydroxytryptamine (5-HT) levels to predict postoperative liver dysfunction and morbidity in patients undergoing liver resection. Based on its striking association with clinical outcome after partial hepatectomy, we thus proposed that IP 5-HT might represent a therapeutic target to accelerate liver regeneration after liver resection.[1] It should be stressed that we did not evaluate the effects of IP 5-HT on tumor development or progression or its effects on viral hepatitis. Pang et al. point to a relevant issue with the potential use of 5-HT which may appear like a double-edge sword for the liver as it has also recently been discussed by Lesurtel et al. in more detail.[2] We agree with Pang et al. that further research is required to determine whether perioperative modification of IP 5-HT levels is of overall benefit in patients undergoing liver resection and that the following aspects should be considered.

First, adverse effects of 5-HT pointed out by Pang et al. have only been described in animal or cell culture experiments and need to be confirmed in humans. Second, these detrimental effects might be probably associated with long-term exposure to 5-HT, while we are hypothesing that short-term perioperative manipulation of IP 5-HT levels may be beneficial after hepatectomy. The therapeutic window to increase IP 5-HT may

be of crucial importance. Based on our data, the most reasonable approach of interfering with IP 5-HT levels to support liver regeneration would presumably be a short-term elevation prior to liver surgery as well as within the first postoperative week. This therapeutic setting will have to be evaluated with respect to potential deleterious effects on the underlying liver disease. In this context, Nozaki et al. documented that the controlled increase of platelets (and therefore presumably available 5-HT) using thrombopoietin, had no proliferative effect on hepatocellular carcinoma in vitro or in vivo.[3] This finding supports the notion that a temporary, perioperative increase of platelet counts and concomitantly 5-HT, might have limited adverse effects on liver cancer.

Most importantly, it should be stated that postoperative liver failure is frequently a fatal complication after liver resection.[4] As specific therapeutic options to accelerate liver regeneration are missing to date, we would strongly argue for evaluating 5-HT as a therapeutic target. A careful definition of treatment indications and therapeutic timing may be key to promote liver regeneration without inducing potential deleterious effects.

References:

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